TOWARD A BIOLOGICAL DEFINITION OF ALZHEIMER'S DISEASE

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2018 National Institute on Aging—Alzheimer's Association (NIA-AA) Research Framework

NIA-AA Research Framework: Toward a biological definition of Alzheimer's disease

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FLASH-BACK : ALZHEIMER'S DISEASE – CRITERES 2011

- **Entité clinico - pathologique**
- Terme « parapluie »
- **Diagnostic définitif post - mortem**
- **In vivo :** Diagnostic de « probabilité »
- Preclinical - MCI - Alzheimer's dementia
- « Syndrome démentiel » : Ni spécifique, ni sensible

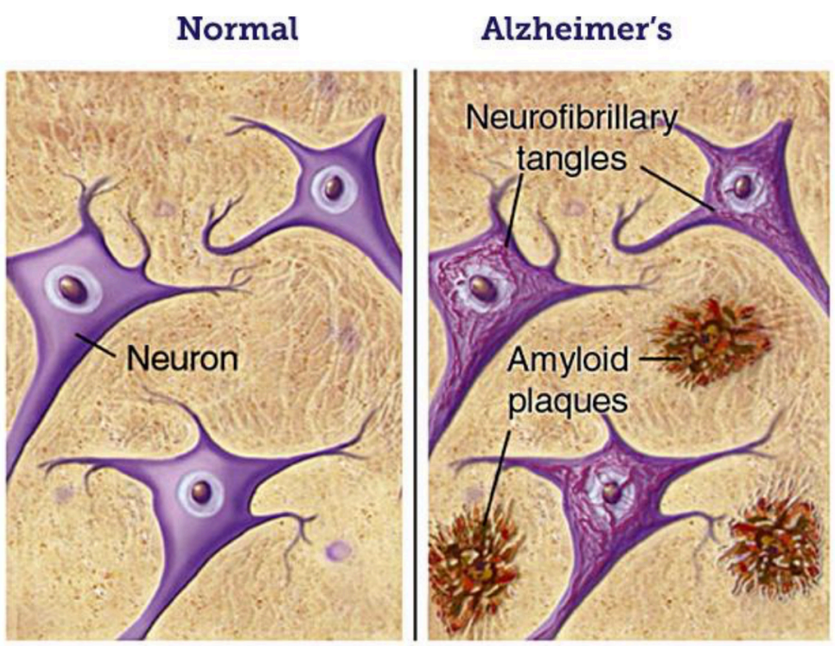
FLASH-BACK : ALZHEIMER'S DISEASE – CRITERES 2011

PROBABLE AD DEMENTIA

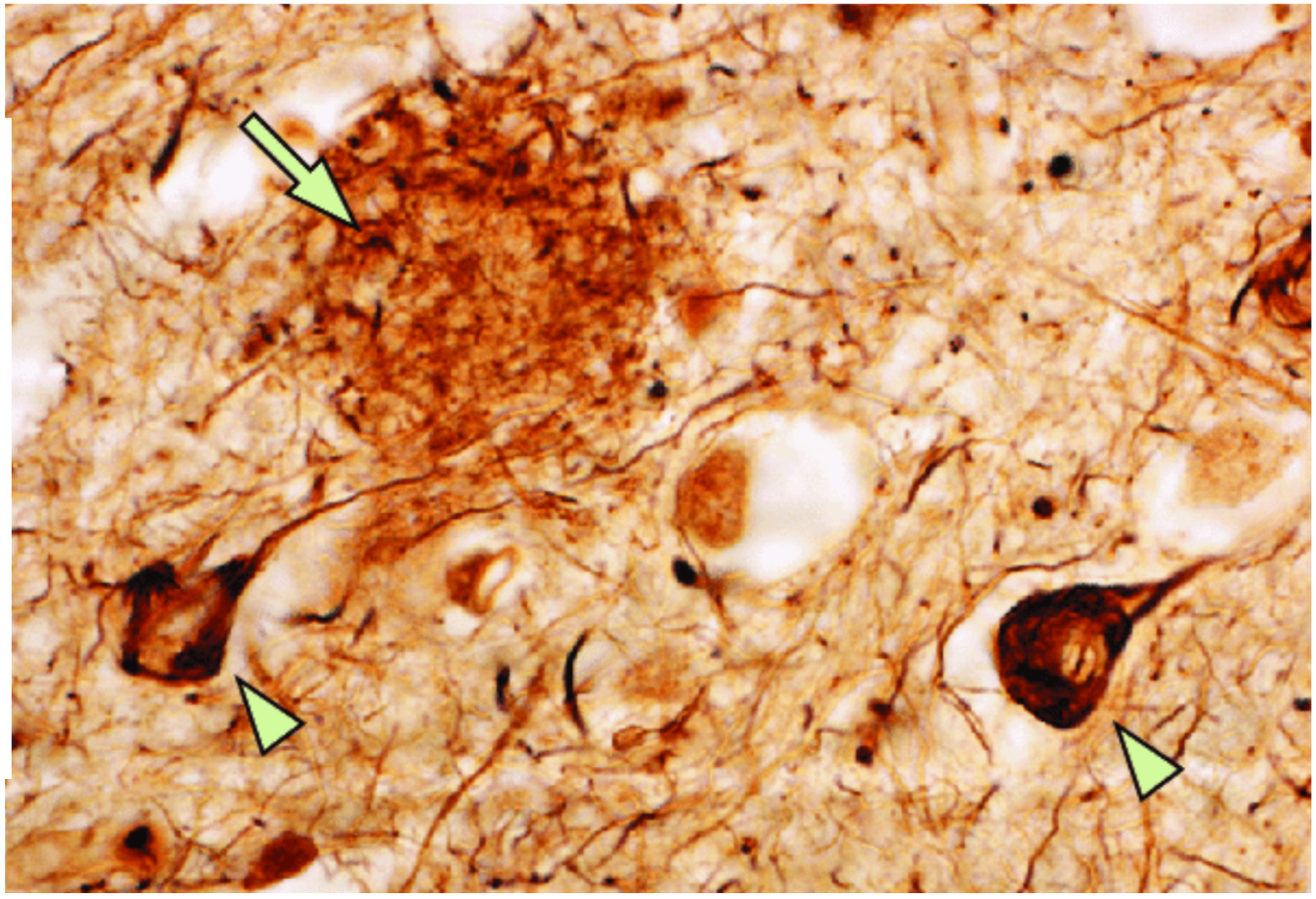
A. Insidious onset. Symptoms have a gradual onset over months to years, not sudden over hours or days;
B. Clear-cut history of worsening of cognition by report or observation; and
C. The initial and most prominent cognitive deficits are evident on history and examination in one of the following categories.
    a. Amnestic presentation: It is the most common syndromic presentation of AD dementia. The deficits should include impairment in learning and recall of recently learned information. There should also be evidence of cognitive dysfunction in at least one other cognitive domain, as defined earlier in the text.
    b. Nonamnestic presentations:
        - Language presentation: The most prominent deficits are in word-finding, but deficits in other cognitive domains should be present.
        - Visuospatial presentation: The most prominent deficits are in spatial cognition, including object agnosia, impaired face recognition, simultanagnosia, and alexia. Deficits in other cognitive domains should be present.
        - Executive dysfunction: The most prominent deficits are impaired reasoning, judgment, and problem solving. Deficits in other cognitive domains should be present.

(1) McKhann G., Knopman D., Chertkow H. et al., The diagnosis of dementia due to Alzheimer's disease : Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease, *Alzheimers Dement.*, 2011, **7(3)**, 263-269

RAPPELS : ANATOMOPATHOLOGIE – GOLD STANDARD



BrightFocus® Foundation
Cure in Mind. Cure in Sight.



L'ÈRE DES BIO MARQUEURS

AMYLOÏDE	P-TAU	NEURO - DÉGÉNÉRESCENCE
A	**T**	**N**
↓ $A\beta_{42}$ (LCR) Amyloïde - PET	↑ P-tau (LCR) Tau - PET	↑ Tau (LCR) FDG - PET Atrophie (IRM)

PROFIL DE BIOMARQUEURS

AT(N) profiles	Biomarker category	
A-T-(N)-	Normal AD biomarkers	
A+T-(N)-	Alzheimer's pathologic change	Alzheimer's continuum
A+T+(N)-	Alzheimer's disease	
A+T+(N)+	Alzheimer's disease	
A+T-(N)+	Alzheimer's and concomitant suspected non Alzheimer's pathologic change	
A-T+(N)-	Non-AD pathologic change	
A-T-(N)+	Non-AD pathologic change	
A-T+(N)+	Non-AD pathologic change	

« COMBINED STAGING »

		Cognitive stage		
		Cognitively Unimpaired	**Mild Cognitive Impairment**	**Dementia**
Biomarker Profile	**$A^- T^-(N)^-$**	normal AD biomarkers, cognitively unimpaired	normal AD biomarkers with MCI	normal AD biomarkers with dementia
	$A^+ T^-(N)^-$	Preclinical Alzheimer's pathologic change	Alzheimer's pathologic change with MCI	Alzheimer's pathologic change with dementia
	$A^+ T^+ (N)^-$ **$A^+ T^+(N)^+$**	Preclinical Alzheimer's disease	Alzheimer's disease with MCI(Prodromal AD)	Alzheimer's disease with dementia
	$A^+ T^- (N)^+$	Alzheimer's and concomitant suspected non Alzheimer's pathologic change, cognitively unimpaired	Alzheimer's and concomitant suspected non Alzheimer's pathologic change with MCI	Alzheimer's and concomitant suspected non Alzheimer's pathologic change with dementia
	$A^- T^+(N)^-$ **$A^- T^-(N)^+$** **$A^-T^+(N)^+$**	non-Alzheimer's pathologic change, cognitively unimpaired	non-Alzheimer's pathologic change with MCI	non-Alzheimer's pathologic change with dementia

TAKE – HOME MESSAGE

- Le « syndrome démentiel » n'est pas suffisant pour poser un diagnostic de maladie d'Alzheimer
- La maladie d'Alzheimer évolue d'une définition « anatomo-clinique » à une définition « biologique »
- Il faut distinguer le profil biologique du profil clinique
- La place des bio marqueurs dans les traitements futurs ?